Key messages

- The influence of secondary care establishments on prescribing in primary care has not been fully measured
- Using glyceryl trinitrate buccal tablets as an example, this study measured the "hospital effect" in different catchment areas in a family health services authority
- Catchment area was the single most important variable in predicting prescribing levels
- A statistical model comprising catchment area, urbanity, number of partners in a practice, and a deprivation score explained over 47% of the variation in the prescribing of glyceryl trinitrate buccal tablets

"That's true, those young men can be very energetic..." said Miss Scarlett, thoughtfully. "I suppose that the activity of drug representatives is a possible source of confounding."

"But the same representative covers the whole of Buccalshire!" said Dr Watson.

"In addition, it's not possible to tell from PACT data whether treatment was started by a hospital clinician or the general practitioner—that is, whether a prescription was hospital initiated or not. This is another potential confounder," said Miss Scarlett.

"I find all this a bit difficult to digest," ruminated Dr Watson.

"It's alimentary, my dear Watson!" Colonel Mustard exclaimed. "The most important variable in predicting glyceryl trinitrate buccal tablet prescribing is the influence of secondary care, and this seems to be confirmed by the drug company sales data" (table 4).

"Perhaps you should eat more slowly?" suggested Miss Scarlett helpfully.

Epilogue

Miss Scarlett, Colonel Mustard, and Dr Watson set out to discover why the prescribing of glyceryl trinitrate buccal tablets in Buccalshire was so high. The most significant factor seemed to be the influence of prescribing at the interface between secondary and primary care, in particular, the effect of hospital X.

Previous work has shown that the buccal formulation of nitroglycerin is as effective as the intravenous formulation of isosorbide dinitrate,[21] and consequently use of the buccal formulation in hospitals is a sensible economic choice. Thus, this was probably not an attempt to cost shift prescribing to primary care, but it may be a case of general practitioners "learning by demonstration."[13] Whatever the cause of this "hospital effect," the result on primary care is a significant cost burden on Buccalshire Family Health Services Authority.

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Effect of colour of drugs: systematic review of perceived effect of drugs and of their effectiveness

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Abstract

***Objectives*—To assess the impact of the colour of a drug's formulation on its perceived effect and its effectiveness and to examine whether antidepressant drugs available in the Netherlands are different in colour from hypnotic, sedative, and anxiolytic drugs.**

***Design*—Systematic review of 12 published studies. Six studies examined the perceived action of different coloured drugs and six the influence of the colour of a drug on its effectiveness. The colours of samples of 49 drugs affecting the central nervous system were assessed using a colour atlas.**

***Main outcome measures*—Perceived stimulant action versus perceived depressant action of colour of drugs; the trials that assessed the effect of drugs in different colours were done in patients with different diseases and had different outcome measures.**

***Results*—The studies on perceived action of coloured drugs showed that red, yellow, and orange are associated with a stimulant effect, while blue and green are related to a tranquillising effect. The trials that assessed the impact of the colour of drugs on their effectiveness showed inconsistent differences between colours. The quality of the**

methods of these trials was variable. Hypnotic, sedative, and anxiolytic drugs were more likely than antidepressants to be green, blue, or purple.

***Conclusion*—Colours affect the perceived action of a drug and seem to influence the effectiveness of a drug. Moreover, a relation exists between the colouring of drugs that affect the central nervous system and the indications for which they are used. Research contributing to a better understanding of the effect of the colour of drugs is warranted.**

Introduction

The response to drug treatment is not simply a reflection of its chemical compounds. Extraneous factors may considerably influence the size of a treatment effect.[1] Factors such as the reputation of the doctor, the patient's attitude towards the expected benefit, treatment mode, and credibility of the treatment might influence patients' expectancies and therefore the therapeutic outcome.

Most colours have universal meanings in a wide variety of cultures, red generally being considered strong and active, and blue and green to be associated with good.[2] The colour of drug formulations might cause different expectations in patients, and could therefore produce different therapeutic effects. In this study we sought the answers to three questions: Are formulations of different colours perceived as equally active? Do different coloured formulations of the same drug produce a different effect in randomised clinical trials? Is the colour of available hypnotics, sedatives, and anxiolytics systematically different from that of antidepressants in the Netherlands? We systematically reviewed published work to answer the first two questions, and we assessed the colours of drug samples to answer the last.

Materials and methods

Search for publications—Relevant publications were located by computer searches of Medline (1966-95) with medical subject heading colour and pill, tablet, medication, capsule, or drug in the title or abstract. Embase (1974-95) and ClinPSYC (1980-94) were searched with similar strategies. Other publications were found by reviewing reference lists, through correspondence with authors of books and articles on related subjects, and through correspondence with pharmaceutical companies. The *Science Citation Index* was used for prospectively identifying studies that cited previous ones.

Assessment of colours—To assess the colour of oral drugs that affect the central nervous system and are available in the Netherlands we approached all Dutch manufacturers of hypnotic, sedative, anxiolytic, or antidepressant drugs. They were asked for the most frequently prescribed dose of their product and to send us one example of this. In case a company did not respond, prescription details were derived from Intercontinental Medical Statistics,[3] and colour was assessed in the hospital pharmacy. Colour of products was assessed using the Reichs Ausschuss für Lieferbedingungen design colour atlas.[4] Drugs affecting the central nervous system were classed as sedative drugs (hypnotics, sedatives, and anxiolytics) or antidepressants, and the distribution of colours over the two groups was assessed.

Results

PERCEIVED ACTION OF COLOURED DRUG FORMULATIONS

We found six publications that studied the perceived action of coloured drugs.[5-10] Four studies assessed the expected effect of different colours in terms of stimulant or antidepressant and depressant or tranquillising.[5-8] Red, yellow, and orange were related to a stimulant effect, while blue and green were associated with a tranquillising effect (table 1). One study found that the colour of the drug affected the perceived site of action, white being most common for general drugs, red and scarlet for cardiovascular and blood or lymphatic systems, and tan, beige, and burnt orange for skin.[9] Another investigation studied the perceived strength of coloured capsules. Red and black were perceived as strong and white as weak.

EFFECTS OF COLOURED DRUG FORMULATIONS

Six trials investigated the influence of the colour of drug formulation on the specific effect.[11-16] The methodological quality of these trials, assessed using a previously reported 10 point rating scale,[1] was seven points for two trials[11 12], six and a half points for one trial,[13] and less than five points for three trials.[14-16] The table with scores and the items of methodological quality are available from AJMdeC and on the *BMJ*'s worldwide web page (http://www.bmj.com/bmj/).

All trials had different designs and different outcome measurements, so a meta-analysis was not possible. Overall, the results indicated differences between colours, but a consistent trend could not be detected.

In a double blind crossover study Cattaneo *et al* gave orange and blue placebos to 120 inpatients awaiting minor surgery who thought that they were receiving tranquillisers.[11] In an analysis excluding patients with no preference, they showed that 26 out of 42 men (62%) preferred orange whereas 33 out of 54 women (61%) preferred blue capsules. Furthermore, they reported that the efficacy data were consistent with the expressed preference.

In a crossover study, Schapira *et al* randomly allocated 48 patients with anxiety symptoms to oxazepam administered in three different colours.[12] Every patient received one week's treatment with each colour. Although statistical significance was not reached, anxiety symptoms were most improved with green and depressive symptoms responded best to yellow.

In a single blind experiment showing the effect of placebo Blackwell *et al* asked 100 medical students to participate in an experiment in which they they would receive either a sedative or stimulant drug.[13] All of the 56 students who volunteered in fact received either a blue or a pink placebo. Subjects taking the blue placebos felt less alert (66%) than those taking the pink (26%) and also more drowsy (72% *v* 37% respectively).

In a randomised crossover study reported by Luchelli *et al* 96 patients admitted for elective surgery were randomised to receive either a hypnotic agent or placebo on

Table 1—*Summary of studies investigating perceived potencies* of different coloured drugs*

First author	Blue	Green	Orange	Red	Yellow	White
Buckalew[5]	Depressant	Analgesic	Stimulant	—	Stimulant	Analgesic
Buckalew[6]	—	Depressant	Stimulant	—	—	Stimulant
Jacobs[7]	Depressant	—	—	Stimulant	Stimulant	—
Sebellico[8]	Depressant	Depressant	Stimulant	Stimulant	Stimulant	Depressant

*Depressant also includes hypnotic and tranquillising; stimulant includes antidepressant.

Table 2—*Colours of sedative (hypnotics, sedatives, and anxiolytics) and antidepressant drugs*

Category	Red, orange, yellow	Green, blue, purple	White	Multicoloured	Total
Sedative	5	9	16	1	31
Antidepressant	8	1	7	2	18
Total	13	10	23	3	49

the first night.[14] On the second night all patients received the other study drug, which was the same colour as that on the night before. Two colours were tested, blue and orange. Patients taking blue capsules reported falling asleep significantly more quickly than those taking the orange capsules (103 minutes *v* 135 minutes; $P<0.05$), and those taking the blue capsules slept longer (379 minutes *v* 346 minutes; $P<0.01$).

In a large double blind trial of an analgesic after dental surgery Nagao *et al* found that 79% of patients experienced adequate pain relief with red tablets, whereas 73% of patients reported adequate pain relief with white tablets.[15]

In a crossover trial reported by Huskisson 24 patients with rheumatoid arthritis received red, blue, green, or yellow drugs.[16] Three analgesics were tested against placebo. The red placebo was as effective in relieving pain as any of the active drugs. Blue and green placebos were average pain relievers. Colour did not change the effectiveness of the active drugs.

COLOURS OF ORAL DRUGS AFFECTING THE CENTRAL NERVOUS SYSTEM

We assessed the colour of 49 oral drugs affecting the central nervous system (table 2). Sedatives in comparison with antidepressants were more often green, blue, or purple (Fisher exact P value: 0.029 when white and multicoloured drugs were excluded from the analysis and 0.035 when they were included). However, colours were not consistent in the two categories. A list of all 49 drugs assessed is available from AJMdeC and on the *BMJ*'s worldwide web page.

Discussion

Our review shows that little research has been done to study the effect of coloured drug formulations. Studies on the perceived effect of colour show that red, orange, and yellow tablets are best for stimulant drugs and that blue and green tablets are best for sedative drugs. The studies assessing the influence of colour on the effectiveness of a drug did not find a general trend favouring one or more colours. Our assessment of the colours used in oral drugs affecting the central nervous system indicates that sedatives are more often green, blue, or purple than are antidepressants.

There might be several explanations why different colours have different effects. Colour itself might have direct psychophysiological effects. Moreover, if the colour of the drug parallels the perceived action patients might better comply, resulting in a better outcome. The colour of a drug is not the only perceptual characteristic that could influence patients' response to the drug. Preparation form (capsule or tablet) and size are other factors that may affect a therapeutic outcome. Buckalew and Coffield found that capsules are perceived as stronger compared to tablets.[5] Similarly, in a clinical trial comparing chlordiazepoxide capsules with tablets Hussain concluded that in the treatment of anxiety the overall response was better when patients were treated with capsules.[17]

Patients taking more than one drug might recognise different drugs better if they are in various colours. This probably reduces accidental poisonings. Accidental poisoning has been reported often, from as early as 1956.[18] After this report in 1956 Jolly and Forrest suggested that drugs should be different from each other and should not resemble sweets to prevent accidental poisoning in children.[19]

We approached several pharmaceutical companies for relevant publications. Although they were greatly interested and helpful, they did not find many publications on the effects of coloured drugs. One article on perceived effects of coloured drugs was retrieved this way,[8] and one company suggested that research had been done with their products. Pharmaceutical companies might be more interested in different colours for marketing purposes than for efficacy. However, the distribution of colours over the sedative and antidepressant medication of different companies showed a relation between colour and category that suggests that the colour of drugs might be determined by factors other than marketing alone.

Key messages

- Red, yellow, and orange drug formulations are perceived as stimulant and blue and green as tranquillising
- The colour of a drug seems to influence its effectiveness, but consistent trends are not apparent
- Hypnotic, sedative, and anxiolytic drugs available in the Netherlands are more likely than antidepressants to be green, blue, or purple
- Research contributing to a better understanding of the effect of the colour of drugs is warranted

CONCLUSION

In conclusion, little research has been carried out investigating the effect of coloured drugs, but the available evidence suggests that green and blue may have more sedative effects and red and orange may have more stimulant effects. Research contributing to a better understanding of the effect of coloured medication is certainly warranted.

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